

CLAIMS:

What is claimed is:

- 5 1. An siRNA-cochleate composition comprising:
 a cochleate; and
 an siRNA associated with the cochleate.
2. The siRNA-cochleate composition of claim 1, wherein the siRNA comprises
10 at least one mismatch.
3. The siRNA-cochleate composition of claim 1, wherein the siRNA comprises
 at least one substitution.
- 15 4. The siRNA-cochleate composition of claim 1, wherein the siRNA is about 21-
 23 nucleotides long.
5. The siRNA-cochleate composition of claim 1, wherein the siRNA mediates
 RNA interference against a target mRNA.
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6. The siRNA-cochleate composition of claim 5, wherein the target mRNA
 expresses a protein selected from the group consisting of: a cancer protein, a virus
 protein, an HIV protein, a fungus protein, a bacterial protein, an abnormal cellular
 protein, a normal cellular protein.
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7. The siRNA-cochleate composition of claim 1, further comprising a second
 siRNA directed against a second target mRNA.
8. The siRNA-cochleate composition of claim 1, wherein the cochleate
30 comprises a negatively charged lipid component and a multivalent cation component.
9. The siRNA-cochleate composition of claim 1, wherein the siRNA is
 complexed with a transfection agent prior to contacting the liposomes.

10. The siRNA-cochleate composition of claim 9, wherein the transfection agent is a polycationic transfection agent.

11. The siRNA-cochleate composition of claim 9, wherein the transfection agent is polyethylenimine (PEI) or a derivative thereof.

12. The siRNA-cochleate composition of claim 1, further comprising at least one additional cargo moiety.

13. The siRNA-cochleate composition of claim 1, further comprising an aggregation inhibitor.

14. A method of administering an siRNA to a host comprising: administering a biologically effective amount of an siRNA-cochleate composition to a host comprising a cochleate and an siRNA associated with the cochleate.

15. The method of claim 14, wherein the siRNA is delivered from the cochleate to a cell in the host.

16. The method of claim 15, wherein the siRNA is delivered into a cytosol compartment of the cell.

17. The method of claim 14, wherein the siRNA mediates RNA interference against a target mRNA in the host.



18. The method of claim 14, wherein target mRNA expression in the host is reduced by at least about 50%.

19. The method of claim 11, wherein target protein synthesis in the host is reduced by at least about 10%.

20. The method of claim 11, wherein target protein synthesis in the host is reduced by at least about 50%.

21. The method of claim 11, wherein the host is a cell, a cell culture, an organ, tissue, or an animal.
22. The method of claim 11, comprising the step of examining the function of the target mRNA or protein expressed by the target mRNA in the host.
23. A method of treating a subject having a disease or disorder associated with expression of a target mRNA, comprising: administering to a subject a therapeutically effective amount of an siRNA-cochleate composition, comprising a cochleate and an siRNA against a target mRNA associated with a disease or disorder, such that the disease or disorder is treated.
24. The method of claim 23, wherein the disease or disorder is selected from the group consisting of: a neurological disorder associated with aberrant or unwanted gene expression, schizophrenia, obsessive compulsive disorder (OCD), depression, a bipolar disorder, Alzheimer's disease, Parkinson's disease, a lysosomal storage disease, Fabry's disease, Gaucher's Disease, Type I Gaucher's Disease, Farber's disease, Niemann-Pick disease (types A and B), globoid cell leukodystrophy (Krabbe's disease), metachromic leukodystrophy, multiple sulfatase deficiency, sulfatidase activator (*sap-B*) deficiency, *sap-C* deficiency, GM1-gangliosidosis, Tay-Sachs disease, Tay-Sachs B1 variant, Tay-Sachs AB variant, Acid Maltase Deficiency, Mucopolysaccharidosis, Sandhoff's disease, a cancer, a cell proliferative disorder, a blood coagulation disorder, Dysfibrinogenaemia, hemophilia (A and B), dermatological disorders, hyperlipidemia, hyperglycemia, hypercholesterolemia, obesity, acute and chronic leukemias and lymphomas, sarcomas, adenomas, a fungal infection, a bacterial infection, a viral infection, an autoimmune disorder, systemic lupus erythematosus, multiple sclerosis, myasthenia gravis, autoimmune hemolytic anemia, autoimmune thrombocytopenia, Grave's disease, allogenic transplant rejection, rheumatoid arthritis, ankylosing spondylitis, psoriasis, scleroderma, carcinomas, epithelial cancers, small cell lung cancer, non-small cell lung cancer, prostate cancer, breast cancer, pancreatic cancer, hepatocellular carcinoma, renal cell carcinoma, biliary cancer, colorectal cancer, ovarian cancer, uterine cancer, melanoma, cervical cancer, testicular cancer, esophageal cancer, gastric cancer, mesothelioma, glioma, glioblastoma, pituitary adenomas, inflammatory diseases, osteoarthritis,

atherosclerosis, inflammatory bowel diseases (Crohns and ulcerative colitis) , uveitis, eczema, chronic rhinosinusitis, asthma, a hereditary disease, cystic fibrosis, and muscular dystrophy.

- 5 25. A method of forming an siRNA-cochleate composition comprising:
precipitating a liposome and an siRNA to form an siRNA-cochleate. 
26. The method of claim 25, comprising adjusting the pH of the siRNA.
- 10 27. The method of claim 25, comprising charging the base pairs of the siRNA.
28. The method of claim 25, wherein the siRNA is complexed with a transfection agent prior to precipitating.
- 15 29. The method of claim 28, wherein the transfection agent is mixed with the liposomes prior to adding the siRNA.
30. The method of claim 28, wherein the transfection agent is PEI or a derivative thereof or other polyvalent cation.
- 20 31. The method of claim 25, comprising using an elevated amount of calcium for precipitating the liposome and the siRNA.
32. The method of claim 25, comprising the step of extruding the liposome an the siRNA prior to precipitation.
- 25 33. The method of claim 25, wherein the siRNA-liposome is prepared by adding a chelating agent to a cochleate to form a liposome in the presence of siRNA.
- 30 34. A morpholino-cochleate composition comprising: 
a cochleate; and
a morpholino oligonucleotide associated with the cochleate.

35. The morpholino-cochleate composition of claim 34, wherein the morpholino oligonucleotide is an antisense morpholino oligonucleotide.
36. The morpholino-cochleate composition of claim 34, wherein the morpholino oligonucleotide comprises at least one mismatch.
37. The morpholino-cochleate composition of claim 34, wherein the morpholino oligonucleotide is about 18-25 nucleotides long.
38. The morpholino-cochleate composition of claim 34, wherein the morpholino oligonucleotide mediates inhibition of translation of a target mRNA.
39. The morpholino-cochleate composition of claim 34, wherein the morpholino oligonucleotide is directed against the synthesis of a protein.
40. The morpholino-cochleate composition of claim 34, wherein the cochleate comprises a negatively charged lipid component and a cation component.
41. The morpholino-cochleate composition of claim 34, further comprising at least one additional cargo moiety.
42. The morpholino-cochleate composition of claim 34, further comprising an aggregation inhibitor.
43. The morpholino-cochleate composition of claim 34, further comprising a second morpholino oligonucleotide directed against the synthesis of the protein or a second protein.
44. A method of administering a morpholino oligonucleotide to a host comprising: administering a biologically effective amount of a morpholino-cochleate composition to the host comprising a cochleate and a morpholino oligonucleotide associated with the cochleate.

45. The method of claim 44, wherein the morpholino oligonucleotide is released from the cochleate into a cell in the host.
46. The method of claim 44, wherein the morpholino oligonucleotide mediates
5 inhibition of translation of a target mRNA.
47. The method of claim 44, wherein target mRNA expression in the host is reduced by at least about 50%.
- 10 48. The method of claim 44, wherein target protein synthesis in the host is reduced by at least about 10%.
49. The method of claim 44, wherein target protein synthesis in the host is reduced by at least about 50%.
- 15 50. The method of claim 44, wherein the host is a cell, a cell culture, an organ, tissue, or an animal.
51. The method of claim 44, wherein the morpholino oligonucleotide is delivered
20 into a cytosol compartment of a cell.
52. A method of forming a morpholino-cochleate composition comprising:
precipitating a liposome and a morpholino to form a morpholino-cochleate. ✓
- 25 53. The method of claim 52, comprising adjusting the pH of the morpholino.
54. The method of claim 52, comprising charging the base pairs of the morpholino.
- 30 55. The method of claim 52, comprising adjusting the pH of the morpholino to induce a charge in the morpholino.
56. The method of claim 52, comprising adjusting the pH of the morpholino to between about 8.0 and about 9.0.

57. The method of claim 52, comprising using an elevated amount of calcium for precipitating the liposome and the morpholino.
- 5 58. The method of claim 52, comprising the extruding the liposome and the morpholino prior to precipitation.
59. The method of claim 52, wherein the liposome is prepared from addition of a chelating agent to a cochleate to form a liposome in the presence of morpholino.
- 10 60. The method of claim 52, further comprising adding at least one additional cargo moiety to the morpholino and the liposome prior to precipitating.
61. The method of claim 52, further comprising adding an aggregation inhibitor to
15 the morpholino and the liposome prior to precipitating.
62. A method of treating a subject having a disease or disorder associated with expression of a target mRNA, comprising: administering to a subject a therapeutically effective amount of an morpholino-cochleate composition, comprising
20 a cochleate and an siRNA against a target mRNA associated with a disease or disorder, such that the disease or disorder is treated.
63. The method of claim 62, wherein the disease or disorder is selected from the group consisting of: a neurological disorder associated with aberrant or unwanted
25 gene expression, schizophrenia, obsessive compulsive disorder (OCD), depression, a bipolar disorder, Alzheimer's disease, Parkinson's disease, a lysosomal storage disease, Fabry's disease, Gaucher's Disease, Type I Gaucher's Disease, Farber's disease, Niemann-Pick disease (types A and B), globoid cell leukodystrophy (Krabbe's disease), metachromic leukodystrophy, multiple sulfatase deficiency, sulfatidase activator (*sap*-B) deficiency, *sap*-C deficiency, GM1-gangliosidosis, Tay-Sachs disease, Tay-Sachs B1 variant, Tay-Sachs AB variant, Acid Maltase
30 Deficiency, Mucopolysaccharidosis, Sandhoff's disease, a cancer, a cell proliferative disorder, a blood coagulation disorder, Dysfibrinogenaemia, hemophilia (A and B), dermatological disorders, hyperlipidemia, hyperglycemia, hypercholesterolemia,

obesity, acute and chronic leukemias and lymphomas, sarcomas, adenomas, a fungal infection, a bacterial infection, a viral infection, an autoimmune disorder, systemic lupus erythematosus, multiple sclerosis, myasthenia gravis, autoimmune hemolytic anemia, autoimmune thrombocytopenia, Grave's disease, allogenic transplant rejection, 5 rheumatoid arthritis, ankylosing spondylitis, psoriasis, scleroderma, carcinomas, epithelial cancers, small cell lung cancer, non-small cell lung cancer, prostate cancer, breast cancer, pancreatic cancer, hepatocellular carcinoma, renal cell carcinoma, biliary cancer, colorectal cancer, ovarian cancer, uterine cancer, melanoma, cervical cancer, testicular cancer, esophageal cancer, gastric cancer, mesothelioma, glioma, 10 glioblastoma, pituitary adenomas, inflammatory diseases, osteoarthritis, atherosclerosis, inflammatory bowel diseases (Crohn's and ulcerative colitis), uveitis, eczema, chronic rhinosinusitis, asthma, a hereditary disease, cystic fibrosis, and muscular dystrophy.